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### **REMARKS**

### **Status of the Claims**

Claims as Filed

Claims 1 to 9 are pending in the specification as filed.

Claims canceled, added and amended

In the instant preliminary amendment, Applicants canceled claims 6 and 7, amended claims 1 to 5 and 8, and added new claims 10 and 11. Thus, after entry of the instant amendment, claims 1 to 5 and 8 to 11 will be pending.

# **Support for the Claim Amendments**

The specification sets forth an extensive description of the invention in the new and amended claims.

## CONCLUSION

In view of the foregoing remarks and the instant amendment, it is believed that the all claims pending in this application (after entry of the instant amendment) are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If any additional necessary fee is required, the Commissioner is authorized to deduct such a fee from the undersigned's Deposit Account No. 06-1050. Please credit any overpayments to the above-noted Deposit Account.

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If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

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# **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Applicant: Nishino, N., et al.

Art Unit : to be assigned Examiner : to be assigned

Serial No.: to be assigned

Filed : August 31, 2001

Title : NOVEL CYCLIC TETRAPEPTIDE DERIVATIVES AND

PHARMACEUTICAL USES THEREOF

# In The Claims:

Claims 6 and 7 have been canceled.

Claim 1 has been amended as follows:

1. (Amended) A cyclic tetrapeptide derivative <u>comprising a</u> [represented by the following] general formula <u>selected from the group consisting of (I), (I'), (I''), (I''') [or] and a pharmaceutically acceptable salt thereof:</u>

$$\begin{array}{c|c} & & & & \\ & & & & \\ & & & & \\ R_{22} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

Preliminary Ame hent

VERSION WITH MARKINGS TO SHOW CHANGES MADE

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$$R_{22}$$
 $R_{21}$ 
 $R_{12}$ 
 $R_{12}$ 
 $R_{12}$ 
 $R_{11}$ 
 $R_{12}$ 
 $R_{11}$ 
 $R_{12}$ 
 $R_{11}$ 
 $R_{12}$ 
 $R_{11}$ 

wherein each of  $R_{11}$ ,  $R_{12}$ ,  $R_{21}$  and  $R_{22}$  independently denotes hydrogen, a linear  $C_1$ - $C_6$ -alkyl group to which a non-aromatic cycloalkyl group or an optionally substituted aromatic ring may be attached, or a branched  $C_3$ - $C_6$ -alkyl group to which a non-aromatic cycloalkyl group or an optionally substituted aromatic ring may be attached; and

each of  $R_1$ ,  $R_2$  and  $R_3$  independently denotes a linear  $C_1$ - $C_5$ -alkylene group which may have a  $C_1$ - $C_6$  side chain, in which the side chain may form a condensed ring structure on the alkylene chain;

provided that at least one of  $R_{11}$ ,  $R_{12}$ ,  $R_{21}$  and  $R_{22}$  in general formula (I''') is a cyclohexyl methyl group.

- 2. (Amended) The cyclic tetrapeptide derivative according to claim 1, comprising [which is represented by] said general formula (I), or a pharmaceutically acceptable salt thereof.
- 3. (Amended) The cyclic tetrapeptide derivative according to claim 1, comprising [which is represented by] said general formula (I'), or a pharmaceutically acceptable salt thereof.

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4. (Amended) The cyclic tetrapeptide derivative according to claim 1, comprising [which is represented by] said general formula (I''), or a pharmaceutically acceptable salt thereof.

- 5. (Amended) The cyclic tetrapeptide derivative according to claim 1, comprising [which is represented by] said general formula (I'''), or a pharmaceutically acceptable salt thereof.
- 8. (Amended) A pharmaceutical composition comprising <u>a</u> [the] cyclic tetrapeptide derivative or <u>a</u> pharmaceutically acceptable salt thereof [according to any one of claims] <u>as set forth in claim</u> 1 [to 5 as an active ingredient].

The following new claims have been added:

- 10. A method of inhibiting a histone deacetylase comprising administering to a subject in need thereof a cyclic tetrapeptide derivative or a pharmaceutically acceptable salt thereof as set forth in claim 1, thereby inhibiting a histone deacetylase inhibitor.
- 11. A method of promoting an expression of an MHC class I molecule comprising administering to a subject in need thereof a cyclic tetrapeptide derivative or pharmaceutically acceptable salt thereof as set forth in claim 1, thereby promoting an expression of an MHC class I molecule.

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